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=> fil reg
FILE 'REGISTRY' ENTERED AT 14:07:17 ON 16 APR 2002
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STRUCTURE FILE UPDATES:   15 APR 2002  HIGHEST RN 405259-61-2
DICTIONARY FILE UPDATES:  15 APR 2002  HIGHEST RN 405259-61-2

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the
CAS Registry Numbers that were added to the H/Z/CA/CAplus files between
12/27/01 and 1/23/02.  Use of the P indicator in online and SDI searches
during this period, either directly appended to a CAS Registry Number
or by qualifying an L-number with /P, may have yielded incomplete results.
As of 1/23/02, the situation has been resolved.  Also, note that searches
conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files
incorporating CAS Registry Numbers with the P indicator between 12/27/01
and 1/23/02, are encouraged to re-run these strategies.  Contact the
CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698,
worldwide, or send an e-mail to help@cas.org for further assistance or to
receive a credit for any duplicate searches.

=> d ide can tot

L80  ANSWER 1 OF 4  REGISTRY  COPYRIGHT 2002 ACS
RN   140879-24-9  REGISTRY
CN   Proteinase, multicatalytic (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   26 S Protease
CN   Immunoproteasome
CN   Large multicatalytic protease
CN   Multicatalytic protease
CN   Multicatalytic proteinase
CN   Multicatalytic proteinase complex
CN   Organelle, proteasome
CN   Prosome
CN   Proteasome
CN   Tricorn protease
CN   Tricorn proteinase
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAPLUS, CEN,
       CIN, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            3043 REFERENCES IN FILE CA (1967 TO DATE)
              23 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            3058 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE   1:  136:246130
```

REFERENCE 2: 136:245552

REFERENCE 3: 136:245304

REFERENCE 4: 136:243578

REFERENCE 5: 136:243346

REFERENCE 6: 136:242899

REFERENCE 7: 136:242778

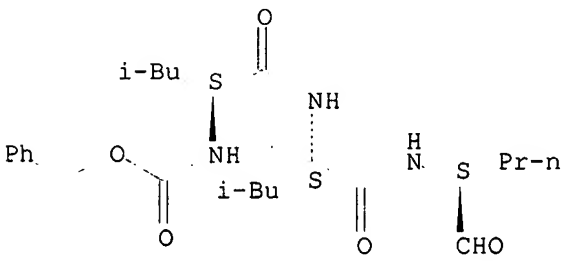
REFERENCE 8: 136:242516

REFERENCE 9: 136:241979

REFERENCE 10: 136:241237

L80 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2002 ACS
RN **133407-86-0** REGISTRY
CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S)-1-formylbutyl]-
(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-(1-formylbutyl)-,
(S)-
OTHER NAMES:
CN MG 115
FS STEREOSEARCH
MF C25 H39 N3 O5
SR CA
LC STN Files: ADISINSIGHT, AGRICOLA, BIOSIS, CA, CAPLUS, CHEMCATS,
TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

27 REFERENCES IN FILE CA (1967 TO DATE)
27 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:41674

REFERENCE 2: 134:331618

REFERENCE 3: 134:324043

REFERENCE 4: 134:161376

REFERENCE 5: 133:317578

REFERENCE 6: 133:172160

REFERENCE 7: 133:144585

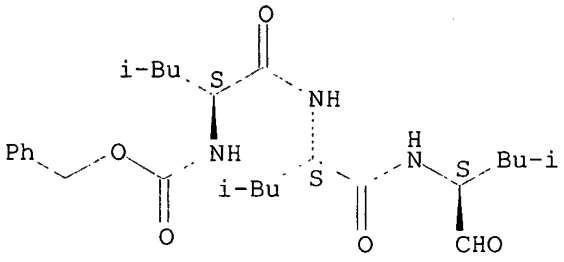
REFERENCE 8: 132:216685

REFERENCE 9: 132:102860

REFERENCE 10: 131:67760

L80 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2002 ACS
RN **133407-82-6** REGISTRY
CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S)-1-formyl-3-methylbutyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-(1-formyl-3-methylbutyl)-, (S)-
OTHER NAMES:
CN MG 132
FS STEREOSEARCH
MF C26 H41 N3 O5
SR CA
LC STN Files: AGRICOLA, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMCATS, DRUGUPDATES, EMBASE, MEDLINE, PROMT, TOXCENTER, USPATFULL

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

115 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
115 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:210571

REFERENCE 2: 136:196263

REFERENCE 3: 136:177734

REFERENCE 4: 136:163836

REFERENCE 5: 136:162808

REFERENCE 6: 136:98078

REFERENCE 7: 136:63751

REFERENCE 8: 136:15055

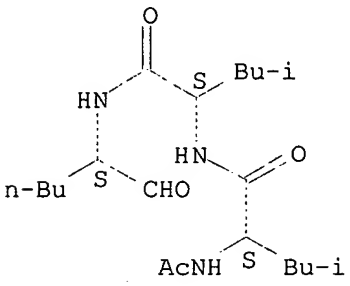
REFERENCE 9: 135:366970

REFERENCE 10: 135:366416

L80 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2002 ACS
RN **110044-82-1** REGISTRY
CN L-Leucinamide, N-acetyl-L-leucyl-N-[(1S)-1-formylpentyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:

CN L-Leucinamide, N-acetyl-L-leucyl-N-(1-formylpentyl)-, (S)-
OTHER NAMES:
CN 6: PN: WO0002548 PAGE: 30 claimed sequence
CN Calpain inhibitor I
CN CI-1 (peptide)
CN MG 101
FS STEREOSEARCH
MF C20 H37 N3 O4
SR CA
LC STN Files: AGRICOLA, BIOSIS, CA, CANCERLIT, CAPLUS, CHEMCATS, CSCHEM, MEDLINE, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

147 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
147 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:210352

REFERENCE 2: 136:196263

REFERENCE 3: 136:179494

REFERENCE 4: 136:147461

REFERENCE 5: 136:63726

REFERENCE 6: 136:48202

REFERENCE 7: 136:33120

REFERENCE 8: 136:31378

REFERENCE 9: 135:316995

REFERENCE 10: 135:205291

=> d his

(FILE 'HOME' ENTERED AT 13:27:40 ON 16 APR 2002)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 13:27:51 ON 16 APR 2002
E MG 132/CN
L1 1 S E3
E MG 115/CN
L2 1 S E3
E MG 101/CN
L3 1 S E3

```
                E C26H41N3O5/MF
L4          30 S E3 AND 46.150.18/RID AND 1/NR
L5          11 S L4 AND FORMYL
L6           8 S L5 AND LEUCYL
L7           6 S L6 NOT ISOLEUCINAMIDE
L8           5 S L7 AND PHENYLMETHOXY
                E C25H39N3O5/MF
L9           2 S E3 AND 46.150.18/RID AND 1/NR AND LEUCINAMIDE AND PHENYLMETHO
                E C20H37N3O4/MF
L10         11 S E3 AND LEUCINAMIDE AND LEUCYL
L11          5 S L10 AND FORMYL
L12          9 S L8,L9,L11 NOT L1-L3
L13          1 S 140879-24-9
L14          3 S L1-L3
                SEL RN
L15          0 S E1-E3/CRN

     FILE 'HCAPLUS' ENTERED AT 13:33:36 ON 16 APR 2002
L16        241 S L14
L17        431 S MG()(132 OR 115 OR 101) OR MG132 OR MG115 OR MG101
L18        157 S CALPAIN INHIBITOR()(1 OR I)
L19        687 S L16-L18
L20         25 S L12
L21       1475 S (PEPTIDE OR PEPTIDYL)(L)(ALDEHYDE OR ALDEHYDIC)
L22          7 S (PEPTIDE OR PEPTIDYL)(L)EPOXY(L)KETONE
L23       3055 S L13
L24       4717 S PROTEASOM?
L25        304 S (26S OR 26 S)(L)(PROTEASE OR PROTEINASE)
L26        774 S MULTICATALYTIC(L)(PROTEASE OR PROTEINASE)
L27         21 S TRICORN(L)(PROTEASE OR PROTEINASE)
L28         49 S IMMUNOPROTEASOM?
L29          9 S IMMUNO PROTEASOM?
L30        105 S PROSOME
L31          2 S IMMUNOPROTEOSOM?
L32          2 S IMMUNO PROTEOSOM?
L33       5020 S L23-L32
L34       1481 S L21,L22
L35        694 S L19,L20
L36       4396 S ALOPEC? OR BALD OR BALDING OR BALDNESS
L37       3041 S SCALP?
L38       5442 S HAIR(L)(LOSS OR LOSE OR LOSING OR LOST OR GROW? OF THIN? OR S
                E HAIR/CT
                E E31+ALL
L39       1419 S E1,E2
                E HAIR/CT
L40       1409 S E6,E8,E9,E13,E15,E16
                E E37+ALL
L41       1329 S E1,E2
                E HAIR GROWTH/CT
                E E7+ALL
                E E1
                E E10+ALL
L42      15395 S E2+NT
                E E9+ALL
L43      18926 S E6,E5+NT
L44        824 S E20+NT
                E HAIR/CT
L45        603 S E24
L46         40 S E26
L47         73 S E32
L48         42 S E39
L49         56 S E42
                E E26+ALL
L50        289 S E2
                E HAIR PREPARATION/CT
L51       4002 S E7,E8,E9,E10,E13,E15-E23
```

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L52        8270 S SHAMPOO?
                E KERATIN/CT
                E E18+ALL
                E E1
                E E17+ALL
L53           3 S L35 AND L36-L52
L54           2 S L53 NOT HYPOXIA
L55           7 S L33 AND L36-L52
L56           6 S L34 AND L36-L52
L57          12 S L54-L56
L58         819 S (26S OR 26 S)(L)(PROTEASOM? OR PROTEOSOM?)
L59           4 S L58 AND L36-L52
L60          12 S L57,L59
                SEL DN 1 4 5 9 10 11 L60
L61           6 S L60 AND E1-E6
                E MUNDY G/AU
L62         259 S E3,E6-E10
                E GARRETT I/AU
L63          53 S E3-E7
L64          55 S E239
L65           7 S E309,E310
                E GOSSINI G/AU
                E ROSSINI G/AU
L66          80 S E3-E16
L67           2 S L35 AND L62-L66
L68           1 S L34 AND L62-L66
L69           4 S L33 AND L62-L66
L70           8 S L61,L67-L69
                E OSTEOSCREEN/PA,CS
L71          13 S E3-E12
L72           3 S L71 AND L33-L35
L73           8 S L70,L72
L74           7 S L73 AND (HAIR OR BALD? OR ALOPEC? OR SHAMPOO OR FOLLIC? OR SH
L75           8 S L73,L74
L76           2 S L75 AND (GROWTH FACTOR)(L)(EPIDERM? OR FIBROBLAST? OR PLATELE
L77           0 S L75 AND (PARATHYROID OR LEUKEM?)
L78           3 S L75 AND GROWTH? FACTOR?
L79           8 S L75,L76,L78
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 14:06:56 ON 16 APR 2002
L80           4 S E1-E4

     FILE 'REGISTRY' ENTERED AT 14:07:17 ON 16 APR 2002

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 14:07:28 ON 16 APR 2002
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FILE COVERS 1907 - 16 Apr 2002  VOL 136 ISS 16
FILE LAST UPDATED: 14 Apr 2002  (20020414/ED)
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This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

=> d all hitstr tot 179

L79 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:300537 HCAPLUS
DN **134:331618**
TI Inhibitors of **proteasomal** activity for stimulating bone and **hair growth**
IN **Mundy, Gregory R.; Garrett, Ross I.; Rossini, G.**
PA **Osteoscreen, Inc., USA**
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-06
ICS A61K038-07; A61K038-13; A61K031-165; A61K031-365; A61K031-4015; A61K031-522; A61P019-00; A61P043-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 62
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001028579	A2	20010426	WO 2000-US41360	20001020
	WO 2001028579	A3	20010920		

W: AU, CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1999-421545 A 19991020
US 2000-558973 A 20000425

AB Compds. that inhibit the activity of NF-.kappa.B or inhibit the activity of the **proteasome** or both promote bone formation and **hair growth** and are thus useful in treating osteoporosis, bone fracture or deficiency, primary or secondary hyperparathyroidism, periodontal disease or defect, metastatic bone disease, osteolytic bone disease, post-plastic surgery, post-prosthetic joint surgery, and post-dental implantation; they also stimulate the prodn. of **hair follicles** and are thus useful in stimulating **hair growth**, including **hair** d., in subject where this is desirable. N-carbobenzyol-Ile-Glu-(OtBu)Ala-Leu-CHO (PSI) in 50% propylene glycol, 10% DMSO, and 40% water was injected daily for 5 days (1mg/kg body wt./day) into the s.c. tissue of mice and the tissue was examd. histol. 16 days later. The no. of **hair follicles** increased and the downward extension of these **hair follicles** into the dermal tissue was noted, which are hallmarks of anagen. There was an obvious increase in size of the **follicle** diam. and the root **sheath** diam.
ST **proteasome** inhibitor **hair** bone **growth** stimulant
IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(I.kappa.B (inhibitor of NF-.kappa.B); inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Periodontium
Tooth
(disease; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT **Hair**
(**follicle**; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Bone, disease
(fracture; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Bone
Hair preparations
(**growth stimulants**; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Dental materials and appliances
(implants; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Bone formation
(inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Bone morphogenetic proteins
Estrogens
Growth factors, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Bone, disease
(metastatic and osteolytic; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT **Growth factors**, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteogenins; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Surgery
(post-plastic; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Hyperparathyroidism
(secondary; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Joint, anatomical
(surgery of; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Osteoporosis
(therapeutic agents; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT 13598-36-2D, Phosphonic acid, alkylidenebis- derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bisphosphonate; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT 67-99-2, Gliotoxin 404-86-4, Capsaicin 6493-05-6, PTX 9035-81-8, Trypsin inhibitor 25769-03-3, PDTC 59865-13-3, Cyclosporin a 65240-86-0, PPM 18 79902-63-9, Simvastatin **110044-82-1** 110115-07-6 133343-34-7, Lactacystin **133407-82-6, MG 132** **133407-86-0, MG 115** 134381-21-8, Epoxomicin 158442-41-2D, PSI, epoxides 179324-22-2, MG

262 179324-69-7, PS 341 336099-20-8 336099-21-9 336608-38-9, Bay 11-7082
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

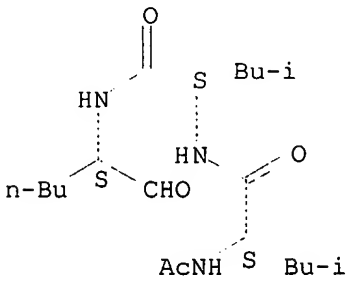
IT 9028-35-7, NADPH-hydroxymethylglutaryl-CoA reductase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors, statins; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT **140879-24-9, Proteasome**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT **110044-82-1 133407-82-6, MG 132**
133407-86-0, MG 115
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

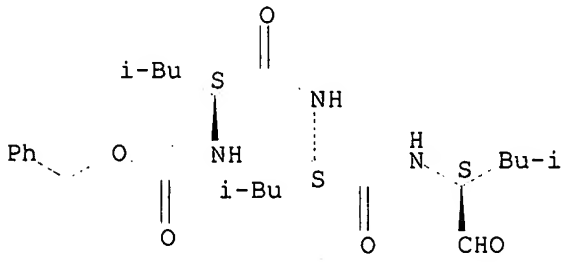
RN 110044-82-1 HCAPLUS
CN L-Leucinamide, N-acetyl-L-leucyl-N-[(1S)-1-formylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



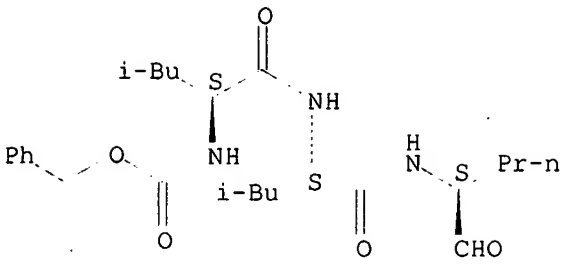
RN 133407-82-6 HCAPLUS
CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S)-1-formyl-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 133407-86-0 HCAPLUS
CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S)-1-formylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **140879-24-9, Proteasome**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)
RN 140879-24-9 HCAPLUS
CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L79 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:741943 HCAPLUS
DN 133:291099
TI Treatment of myeloma bone disease with **proteasomal** and NF-.kappa.B activity inhibitors
IN **Mundy, Gregory R.**
PA **Osteoscreen, Inc., USA**
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-04
ICS A61K031-40; A61K031-166; A61P019-08
CC 1-6 (Pharmacology)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000061167	A2	20001019	WO 2000-US9121	20000407
WO 2000061167	A3	20010111		
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1169049	A2	20020109	EP 2000-921764	20000407
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI US 1999-289229	A	19990409		
WO 2000-US9121	W	20000407		

AB The present invention involves the identification and use of compns. for treating myeloma bone disease. The compns. inhibit **proteasomal** activity and decrease the activity of the transcription factor NF-.kappa.B. Assessment of a candidate compd. for its ability to inhibit prodn. or activity of **proteasomal** enzymes or NF-.kappa.B provides a useful means to identify agents to treat myeloma bone disease.
ST bone myeloma therapy **proteasome** NFkappaB inhibitor; **proteasome** inhibitor bone myeloma therapy; NF kappaB inhibitor bone myeloma therapy
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-.kappa.B (nuclear factor .kappa.B); treatment of myeloma bone disease with **proteasomal** and NF-.kappa.B activity inhibitors)
IT Antitumor agents
(multiple myeloma; treatment of myeloma bone disease with **proteasomal** and NF-.kappa.B activity inhibitors)
IT 5108-96-3 65240-86-0, Ppm-18 158442-41-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of myeloma bone disease with **proteasomal** and NF-.kappa.B activity inhibitors)

IT **140879-24-9, Proteasome**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(treatment of myeloma bone disease with **proteasomal** and NF-.kappa.B activity inhibitors)

IT **140879-24-9, Proteasome**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(treatment of myeloma bone disease with **proteasomal** and NF-.kappa.B activity inhibitors)

RN 140879-24-9 HCAPLUS
CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L79 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:478627 HCAPLUS
DN 133:247623
TI Patterns of gene expression associated with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A
AU Ji, Xiaohui; Chen, Di; Xu, Chi; Harris, Steve E.; **Mundy, Gregory R.**; Yoneda, Toshiyuki
CS Division of Endocrinology and Metabolism, Department of Medicine, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA
SO Journal of Bone and Mineral Metabolism (2000), 18(3), 132-139
CODEN: JBMME4; ISSN: 0914-8779
PB Springer-Verlag Tokyo
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
AB The pluripotent mesenchymal stem cells give rise to osteoblasts, adipocytes, chondrocytes, and myoblasts. The differentiation of these stem cells into each of the mature functional cells may be controlled by a distinctive master gene(s) and is assocd. with temporal and spatial expression of diverse genes. Identification of genes that are expressed during the differentiation of the mesenchymal cells to osteoblasts is, therefore, important to obtain insights into the mol. mechanisms of osteogenesis. The murine undifferentiated mesenchymal cell 3T3-F442A, when treated with the bone morphogenetic protein 2 (BMP-2), a well-characterized inducer of mesenchymal cell differentiation, exhibited both osteoblastic and adipocytic differentiation. Using the SAGE (serial anal. of gene expression) technique, which has been shown to enable quant. anal. of large nos. of genes in a simple and quick manner, the authors obtained 1600 sequence tags representing 2107 individual nucleotide sequences from control and BMP-2-treated 3T3-F442A cells, resp. By comparing the frequency of tag occurrence, the authors found profiles of up- or downregulated genes assocd. with osteoblast or adipocyte phenotype such as type I collagen, osteonectin and OSF-2, or C/EBP.beta., aP2, fatty acid synthase, and lipoprotein lipase, resp., in BMP-2-treated 3T3-F442A cells. The authors' data show that BMP-2 induces not only osteoblastic but also adipocytic differentiation in the 3T3-F442A cells. They also show that the 3T3-F442A cells have bipotentials of differentiating toward osteoblasts and adipocytes. The results, therefore, might explain the inverse correlation between trabecular bone vol. and fat vol. in the bone marrow cavity. The results also suggest that the SAGE may be a useful technique that allows a fast and efficient way to generate global and local views of gene expression assocd. with cellular differentiation of the mesenchymal stem cells.
ST BMP2 gene expression osteoblast adipocyte differentiation
IT Bone morphogenetic proteins

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Antigens
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(AD1; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Chaperonins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(ADP ribosylation factor-like protein 2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(AP-2 (activator protein 2); patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT RNA formation factors
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(C/EBP-.beta. (CCAAT box/enhancer element-binding protein .beta.); patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(Cis2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT G proteins (guanine nucleotide-binding proteins)
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(Gs (adenylate cyclase-stimulating), .alpha.-subunit; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Histones
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(H2A; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Heat-shock proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(HSC73; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(J1; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM

(Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L12; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L22; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L32; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L37a; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(L5; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(OSF-2 (osteoblast-specific factor-2); patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(S16; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(S2, S28; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(S24; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(S29; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(TNF-induced protein complex .gamma.; patterns of gene expression

assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Phosphoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(acidic ribosomal protein P2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Phosphoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(acidic ribosomal, P1; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Phosphoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(acidic ribosomal, P0; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Phosphoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(adducins, human erythrocyte, .alpha.-subunit; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Adipose tissue
(adipocyte, differentiation; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Cell differentiation
(adipocyte; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(calcylin; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(calgizzarins; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Chaperonins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(chaperone CCTB; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Osteoblast
(differentiation; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation,

nonpreparative); PROC (Process)
(human ribosomal protein S20; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(human ribosomal protein S7; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(hydrophobic protein MTF; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(insulin-stimulated eIF-4E binding protein; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(jesolin; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(junB; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(minopontins; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(mitochondrial ATPase inhibitor; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Cell differentiation
(osteoblast; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(p68-c-rel; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Bone formation
(patterns of gene expression assocd. with BMP-2-induced osteoblast and

adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Chloride channel
Fibroblast growth factor receptors
Macrophage migration inhibitory factor
Osteonectin
Ribosomal proteins
Tau factor
Tubulins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(protein for hereditary multiple exostosis; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(rat brain protein; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(rat ribosomal protein L23A; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(rat ribosomal protein S19; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Ribosomal proteins
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(rpA2; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Embryo, animal
(stem cell; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Collagens, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(type I; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT Anion channel
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM

(Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(voltage-dependent 3; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT G proteins (guanine nucleotide-binding proteins)
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(.beta.-subunit; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT **140879-24-9, Proteasome**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(Rc7-I; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT 147014-97-9, CDK4 kinase
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(inhibitor; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT 9004-02-8, Lipoprotein lipase 9007-43-6, Cytochrome c, biological studies 9036-37-7, Aminolevulinic acid dehydrogenase 9045-77-6, Fatty acid synthase 9059-25-0, Lysyl oxidase 9059-32-9, GTPase 60616-82-2, Cathepsin L
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT 9001-16-5, Cytochrome c oxidase
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(subunit VIII; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

IT 37205-63-3, ATP synthase
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(.gamma.-chain precursor and hydrogen-transporting; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT **140879-24-9, Proteasome**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(Rc7-I; patterns of gene expression assocd. with BMP-2-induced osteoblast and adipocyte differentiation of mesenchymal progenitor cell 3T3-F442A)
RN 140879-24-9 HCAPLUS
CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L79 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:53374 HCAPLUS
DN **132:102860**
TI Inhibitors of **proteasomal** activity for stimulating bone and **hair growth**
IN **Mundy, Gregory R.; Garrett, I. Ross; Rossini, G.**
PA **Osteoscreen, USA**
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 1-12 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000002548	A2	20000120	WO 1999-US15533	19990709
W: AL, AM, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SD, SG, SI, SK, TR, TT, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9963109	A1	20000201	AU 1999-63109	19990709
EP 1096924	A1	20010509	EP 1999-933827	19990709
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI US 1998-113947	A1	19980710		
WO 1999-US15533	W	19990709		

AB Compds. that inhibit the activity of NF-.kappa.B or inhibit the activity of the **proteasome** or both promote bone formation and **hair growth** and are thus useful in treating osteoporosis, bone fracture or deficiency, primary or secondary hyperparathyroidism, periodontal disease or defect, metastatic bone disease, osteolytic bone disease, post-plastic surgery, post-prosthetic joint surgery, and post-dental implantation. They also stimulate the

prodn. of **hair follicles** and are thus useful in stimulating **hair growth**, including **hair** d., in subject where this is desirable.

ST **hair** bone **growth** stimulation NFkappaB inhibitor; **proteasome** inhibitor **hair** bone **growth** stimulation

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-.kappa.B (nuclear factor .kappa.B); NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Bone formation
Drug delivery systems
Drug screening
(NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Bone morphogenetic proteins
Estrogens
Growth factors, animal
Hormones, animal, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**, and use with other agents)

IT Antitumor agents
(bone, metastasis; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Skull
(calvarium, calvarial bone **growth** assay; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Cartilage
(cartilage-derived morphogenetic proteins; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**, and use with other agents)

IT Joint, anatomical
(degeneration; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Disease, animal
(dental; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Periodontium
(disease; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT **Hair**
(**follicle**; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Bone, disease
(fracture, and bone deficiency; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Bone
(**growth** promoters; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**, and use with other agents)

IT **Hair preparations**
(**growth stimulants**; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Dental materials and appliances

(implants, post-dental implantation; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Cell differentiation
(inducers; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**, and use with other agents)

IT Bone, neoplasm
(inhibitors, metastasis; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Bone, neoplasm
(metastasis, inhibitors; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(morphogenetic, cartilage-derived; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**, and use with other agents)

IT **Growth factors**, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteogenins; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**, and use with other agents)

IT Bone, disease
(osteolytic; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Isoprenoids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pathway; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT **Peptides**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(peptidic **aldehydes**; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT **Aldehydes**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**peptidyl**; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Surgery
(plastic, post-plastic surgery; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Joint, anatomical
Prosthetic materials and Prosthetics
(post-prosthetic joint surgery; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Hyperparathyroidism
(primary; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**proteasome**; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Bone
(resorption, inhibitors; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**, and use with other agents)

IT Hyperparathyroidism
(secondary; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Osteoporosis
(therapeutic agents; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT Drug delivery systems
(topical; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT 67-99-2, Gliotoxin 404-86-4, Capsaicin 6493-05-6, Pentoxifylline 59865-13-3, Cyclosporin A 79902-63-9, Simvastatin 106096-93-9, Basic **fibroblast growth factor 110044-82-1** 110115-07-6 133343-34-7, Lactacystin **133407-82-6, MG 132 133407-86-0, MG 115** 158442-41-2 179324-22-2, MG 262
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

IT **140879-24-9, Proteasome**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

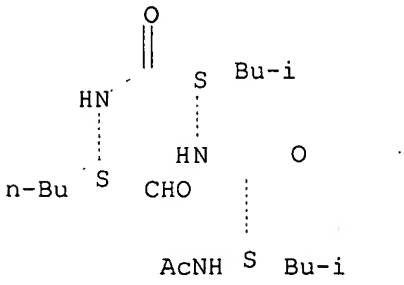
IT 13598-36-2D, Phosphonic acid, bisphosphonates
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and statins; NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**, and use with other agents)

IT **110044-82-1 133407-82-6, MG 132 133407-86-0, MG 115**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)

RN 110044-82-1 HCAPLUS

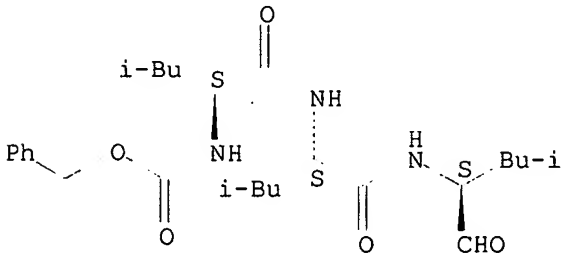
CN L-Leucinamide, N-acetyl-L-leucyl-N-[(1S)-1-formylpentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



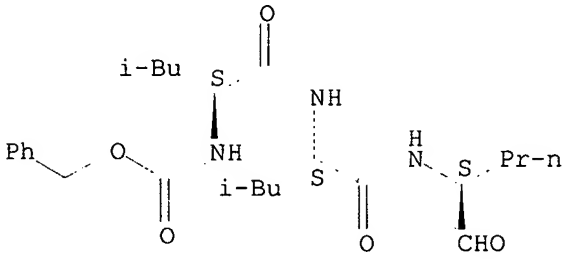
RN 133407-82-6 HCAPLUS
CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S)-1-formyl-3-methylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 133407-86-0 HCAPLUS
CN L-Leucinamide, N-[(phenylmethoxy)carbonyl]-L-leucyl-N-[(1S)-1-formylbutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **140879-24-9, Proteasome**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-.kappa.B inhibitors and inhibitors of **proteasomal** activity for stimulating bone and **hair growth**)
RN 140879-24-9 HCAPLUS
CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L79 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:565931 HCAPLUS
DN **131:183878**
TI Methods for diagnosing and treating autoimmune disease
IN Faustman, Denise L.; Hayashi, Takuma
PA The General Hospital Corporation, USA
SO PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-51
ICS A61K031-70; C12N009-12; G01N033-564; G01N033-573
CC 15-8 (Immunochemistry)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9943346	A1	19990902	WO 1999-US4301	19990225
	W: CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1064020	A1	20010103	EP 1999-911010	19990225
	R: DE, FR, GB				

PRAI US 1998-31629 A 19980227
WO 1999-US4301 W 19990225

AB The invention provides a method of detecting autoimmune disease in a mammal, comprising providing a biol. sample from a mammal and detecting **proteasome** activity, wherein a redn. in **proteasome** activity from a basal state is indicative of autoimmune disease. In addn., the invention encompasses a method of treating an autoimmune disease in a mammal, comprising administering to a mammal suspected of suffering from an autoimmune disease an agent which restores NF-.kappa.B activity in an amt. and for a time sufficient to result in normal NF-.kappa.B activity in the mammal.

ST NFkB restoring agent **proteasome** autoimmune disease

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(200,000-mol.-wt., erythrocyte **proteasome** inhibitor I.kappa.B; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(240,000-mol.-wt. erythrocyte **proteasome** inhibitor CF-2; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Apolipoproteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(B-100; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Intestine, disease
(Crohn's; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Selectins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E-; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Enzymes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E2 (ubiquitin-carrier); detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Muscle, disease
(Eaton-Lambert syndrome; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Kidney, disease
(Goodpasture's syndrome; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Nervous system
(Guillain-Barre syndrome; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Histocompatibility antigens
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(HLA, class II; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Disease, animal
(HLA-II-linked; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Purpura (disease)
(Henoch-Schoenlein's; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Kidney, disease
(IgA nephropathy, idiopathic; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(I.kappa.B (inhibitor of NF-.kappa.B); detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LMP-2 (latent-infection membrane protein 2); detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Transcription factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NF-.kappa.B (nuclear factor .kappa.B), p50 subunit; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Transcription factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NF-.kappa.B (nuclear factor .kappa.B), p52 subunit; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Transcription factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NF-.kappa.B (nuclear factor .kappa.B), p65 subunit; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-.kappa.B (nuclear factor .kappa.B); detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Arthritis
(Reiter's syndrome; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Transcription factors
RL: ADV (Adverse effect, including toxicity); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(STAT, activity redn.; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Transcription factors
RL: ADV (Adverse effect, including toxicity); REM (Removal or disposal); BIOL (Biological study); PROC (Process)
(TFIIH activity redn.; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Kidney, disease
(acute glomerulonephritis; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Hypoparathyroidism
(adult-onset idiopathic; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Nervous system
(amyotrophic lateral sclerosis; detn. of **proteasome** activity

for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Spinal column
(ankylosing spondylitis; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Anemia (disease)
(aplastic, autoimmune; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Artery, disease
(arteritis, giant cell; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Antibodies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(autoantibodies; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Anemia (disease)
(autoimmune hemolytic anemia; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Thyroid gland, disease
(autoimmune thyroiditis; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Addison's disease
Animal tissue
Autoimmune disease
Behcet's syndrome
Celiac disease
Dermatomyositis
Diabetes mellitus
Graves' disease
Hemochromatosis
Lupus erythematosus
Multiple sclerosis
Myasthenia gravis
Psoriasis
Rheumatoid arthritis
Sjogren's syndrome
Vitiligo
(detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Proteins, general, analysis
RL: AMX (Analytical matrix); ANST (Analytical study)
(detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Nucleic acids
RL: AMX (Analytical matrix); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Antibodies
Antisense RNA
Cell adhesion molecules
Cyclins
Interleukin 2
Interleukin 6
Ribozymes
Tumor necrosis factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Heart, disease
(dilated cardiomyopathy; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Endocrine system
(disease, poly-; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Eosinophilia
(eosinophilia-myalgia syndrome; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Skin, disease
(epidermolysis bullosa; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Kidney, disease
(glomerulonephritis, rapidly-progressive; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Transplant and Transplantation
(graft-vs.-host reaction; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Mammal (Mammalia)
(human; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Diabetes mellitus
(insulin-dependent; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Rheumatoid arthritis
(juvenile; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Skin, disease
(linear IgA; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(membrane, Lmp-7; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Heart, disease
(myocarditis; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Sleep
(narcolepsy; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Kidney, disease
(nephrotic syndrome; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p100; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Proteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(p105; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Skin, disease
(pemphigoid; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)

IT Skin, disease
(pemphigus; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Nerve, disease
(peripheral neuropathy; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Autoimmune disease
(polyglandular syndrome type I; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Muscle, disease
(polymyositis; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Erythrocyte
(**proteasome** inhibitors; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Phosphorylation, biological
(protein; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Cell cycle
(restoration; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Connective tissue
(scleroderma, CREST syndrome variant; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Connective tissue
(scleroderma; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Biliary tract
(sclerosing cholangitis; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Muscle, disease
(stiff-man syndrome; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Thyroid gland, disease
(thyroiditis; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT **Alopecia**
(totalis; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Enzymes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ubiquitin-activating; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Enzymes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ubiquitin-conjugating; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Intestine, disease
(ulcerative colitis; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Blood vessel, disease
(vasculitis, necrotizing; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT Hepatitis
(viral, chronic active; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune

diseases)
IT Interferons
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.; detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT **140879-24-9, Proteasome**
RL: ANT (Analyte); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
IT 9026-43-1, Protein kinase 143011-72-7, G-CSF
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Faustman; US 5538854 A 1996 HCAPLUS
(2) Kwon; Diabetes 1998, V47, P583 HCAPLUS
IT **140879-24-9, Proteasome**
RL: ANT (Analyte); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(detn. of **proteasome** activity for diagnosis and NF-.kappa.B-restoring agent for treatment of autoimmune diseases)
RN 140879-24-9 HCAPLUS
CN Proteinase, multicatalytic (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L79 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:746318 HCAPLUS
DN **126:16248**
TI Purification and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy
IN Miller, Douglas K.; Thornberry, Nancy A.; Nicholson, Donald W.; Ali, Ambereen; Vaillancourt, John P.
PA Merck and Co., Inc., USA; Merck Frosst Canada Inc.; Miller, Douglas K.; Thornberry, Nancy A.; Nicholson, Donald W.; Ali, Ambereen; Vaillancourt, John P.
SO PCT Int. Appl., 83 pp
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N009-50
ICS C12N009-64
CC 7-2 (Enzymes)
Section cross-reference(s): 3, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9633268	A1	19961024	WO 1996-US5282	19960417
	W: CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2218679	AA	19961024	CA 1996-2218679	19960417
	EP 822983	A1	19980211	EP 1996-913801	19960417
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 11504209	T2	19990420	JP 1996-531866	19960417
PRAI	US 1995-426557		19950421		
	WO 1996-US5282		19960417		

OS MARPAT 126:16248
AB The present invention is directed to an isolated and purified enzyme designated apopain, methods of using apopain to screen for compds. which modulate the activity of apopain, and compds. identified by the screens. Thus, a poly(ADP-ribose) polymerase cleavage activity (apopain) was detected in progressively apoptotic human osteosarcoma cells. Apopain was

purified and structural anal. showed it to comprise 2 subunits (p17 and p12) proteolytically processed from the 32-kDa CPP32 precursor by cleavage at the Asp28-Ser29 and Asp175-Ser176 positions. A synthetic DNA mol. encoding full-length apopain is prepd. from the purified enzyme. The synthetic apopain-encoding DNA is formulated so as to optimize expression in a variety of recombinant hosts. The DNA clones produce recombinant full-length apopain and derivs. thereof. Purified native apopain and recombinant apopain are useful for identifying modulators of apopain activity and hence modifier of pathol. conditions related to the pro-inflammatory or pro-apoptotic effects of apopain. Thus, the tetrapeptide **aldehyde** inhibitor Ac-YVAD-CHO acts with a Ki of <1 nM, making it among the most potent **peptide aldehydes** known for a cysteine proteinase. The synthesis of Ac-YVAD-CHO is described in detail, and can be generally applied for the synthesis of other **peptidyl** inhibitors. Apopain antisense mols. are useful for therapeutically reducing or eliminating the pro-inflammatory or pro-apoptotic effects of apopain, whereas gene transplantation or gene therapy with apopain is useful for enhancing the pro-inflammatory or pro-apoptotic effects of apopain. These therapies are beneficial in the treatment of immune, proliferative and degenerative diseases including, but not limited to, immune deficiency syndromes (such as AIDS), autoimmune diseases, pathogenic infections, cardiovascular and neurol. injury, **alopecia**, aging, cancer, Parkinson's disease and Alzheimer's disease.

ST human apopain purifn cloning modulation; sequence apopain human

IT Apoptosis
(control of; purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy)

IT Protein sequences
(of human pro-apoptotic cysteine proteinase, apopain)

IT **Aldehydes**, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**peptide aldehydes**; purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by **peptidyl** inhibitors or gene therapy)

IT Antitumor agents
Drugs
Enzyme kinetics
Gene therapy
Michaelis constant
Molecular cloning
Transformation (genetic)
(purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy)

IT Antibodies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy)

IT Synthetic genes
RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy)

IT Antisense DNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy)

IT Aging (animal)
Alopecia
Alzheimer's disease

Autoimmune diseases
Cardiovascular diseases
Immunodeficiency
Infection
Nervous system diseases
Parkinson's disease
(treatment of; purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy)

IT 167976-41-2P, Apopain, prepro- (human) 169443-82-7P 183907-49-5P, Apopain, pro- (human) 183907-50-8P, Apopain (human subunit p17)
RL: BPR (Biological process); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(amino acid sequence; purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy)

IT 183966-65-6P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(chem. synthesis of Ac-DEVD-CHO inhibitor; purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy)

IT 2791-79-9, L-Aspartic acid dibenzyl ester 25952-53-8 30925-18-9
RL: RCT (Reactant)
(chem. synthesis of Ac-DEVD-CHO inhibitor; purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy)

IT 13574-13-5P 80974-42-1P 88224-01-5P, L-Valine allyl ester 160806-33-7P 183966-66-7P 183966-68-9P 183966-70-3P 183966-73-6P 183966-75-8P 183966-77-0P 183966-79-2P 184179-08-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(chem. synthesis of Ac-DEVD-CHO inhibitor; purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy)

IT 169332-60-9
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor; purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy)

IT 143313-51-3
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy)

IT 169592-56-7P, Apopain 169592-57-8P, Apopain, prepro-
RL: BPR (Biological process); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy)

IT 169332-61-0
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(reagent for apopain assay; purifn. and characterization of the human pro-apoptotic cysteine proteinase, apopain, and its modulation by peptidyl inhibitors or gene therapy)

L79 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 1996:637064 HCAPLUS
DN **125:266051**
TI Homology of interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and inhibition of cell death
IN Horvitz, H. Robert; Yuan, Junying; Shaham, Shai

PA Massachusetts Institute of Technology, USA
SO PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-55
ICS A61K038-02; A61K038-07
CC 1-12 (Pharmacology)
Section cross-reference(s): 3, 7, 15
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9625946	A1	19960829	WO 1996-US2473	19960223
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR				
US 5962301	A	19991005	US 1995-394189	19950224
AU 9651336	A1	19960911	AU 1996-51336	19960223

PRAI US 1995-394189 19950224
US 1992-897788 19920612
US 1992-984182 19921120
US 1994-282211 19940711
WO 1996-US2473 19960223

AB Human interleukin-1.beta. convertase (ICE) is structurally similar to the protein encoded by the Caenorhabditis elegans cell death gene ced-3. The nematode ced-3 gene was cloned, sequenced, and characterized by std. techniques of mol. biol. The ced-3 gene has 7 introns with range in size from 54 to 19985 bp, and the ced-3 transcript was trans-spliced to a C. elegans splice leader SL1; the gene encodes a putative protein of 503 amino acids which was very hydrophilic with no significantly hydrophobic region which might be a transmembrane domain. Comparative and mutational analyses of the ced-3 and ICE proteins, together with previous observations, suggest that the Ced-3 protein may be a cysteine protease like ICE and that ICE may be a human equiv. of the nematode cell death gene. Another mammalian protein, the murine NEDD-2 protein, was also found to be similar to Ced-3. The NEDD-2 gene is implicated in the development of the murine central nervous system. On the basis of these findings, novel drugs for enhancing or inhibiting the activity of ICE, ced-3, or related genes are provided. ICE inhibitors such as the **peptide aldehyde** Ac-Tyr-Val-Ala-Asp-CHO or **peptide** chloromethylketone arrest the programmed cell death of chick spinal motoneurons in vitro and in vivo. Such drugs may be useful for treating inflammatory diseases and/or diseases characterized by cell deaths, as well as cancers, autoimmune disorders, infections, and **hair growth** and **hair loss**. Furthermore, such drugs may be useful for controlling pests, parasites, and genetically engineered organisms. Furthermore, novel inhibitors of the activity of ced-3, ICE, and related genes are described which comprise portions of the genes of their encoded products. The ced-3 protein contg. a Cys358.fwdarw.Ala mutation can prevent programmed cell death in C. elegans.

ST cell death inhibition ced3 homolog Caenorhabditis; gene ced3 sequence cell death Caenorhabditis; interleukin convertase homol ced3 NEDD2 protein

IT Gene, animal
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(ICE; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Gene, animal
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(NEDD-2; homol. of human interleukin-1.beta.-convertase with

Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Proteins, specific or class, biological studies
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene NEDD-2; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Proteins, specific or class, biological studies
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene ced-3; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Proteins, specific or class, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene cmrA, from cowpox virus; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Apoptosis
Caenorhabditis elegans
Deoxyribonucleic acid sequences
Inflammation inhibitors
Protein sequences
(homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT **Alopecia**
Infection
Parkinsonism
(treatment of cell death in; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Gene, animal
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(ced-3, homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Virus, animal
(cowpox, CrmA protein as ICE proteinase inhibitor of programmed cell death; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Nerve, disease
(degeneration, treatment of cell death in; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Nervous system
(disease, Friedreich's ataxia, treatment of cell death in; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Nervous system
(disease, Huntington's chorea, treatment of cell death in; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Nervous system
(disease, amyotrophic lateral sclerosis, treatment of cell death in; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Nervous system
(disease, autosomal dominant pure cerebellar ataxia, treatment of cell death in; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Spinal cord

(disease, injury, treatment of cell death in; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Nervous system
(disease, spinocerebellar degeneration, treatment of cell death in; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Heart, disease
(infarction, treatment of cell death in; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Brain, disease
(injury, treatment of cell death in; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Nerve
(motor, inhibition of cell death of; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT **Aldehydes**, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**peptide**, homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT Brain, disease
(stroke, treatment of cell death in; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT 138862-09-6 154690-50-3 154690-61-6, Protein NEDD 2 (mouse reduced)
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT 154250-55-2 154250-83-6 154250-84-7 154690-52-5 154690-55-8
154690-56-9 154690-57-0 154690-58-1 154690-59-2 154690-60-5
154690-73-0 154690-74-1 154690-75-2 154690-76-3 154690-77-4
182513-47-9 182513-48-0 182513-49-1 182513-50-4 182513-51-5
182513-52-6 182513-53-7 182513-54-8 182513-55-9 182513-56-0
182513-57-1 182513-58-2
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT 122191-40-6, Interleukin 1.beta. convertase
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT 143313-51-3 153604-27-4D, **peptide aldehydes** contg.
153604-28-5D, **peptide aldehydes** contg. 153604-29-6D,
peptide aldehydes contg. 153604-30-9D, **peptide**
aldehydes contg. 153604-31-0D, **peptide**
aldehydes contg. 153604-32-1D, **peptide**
aldehydes contg. 153604-33-2D, **peptide**
aldehydes contg.
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT 37353-41-6, Cysteine proteinase 137546-41-9, Proteinase, aspartate-specific
RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use);

BIOL (Biological study); PROC (Process); USES (Uses)
(homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

IT 138861-51-5 153517-58-9 154690-63-8 154690-64-9 154690-65-0
154690-66-1 154690-67-2 154690-68-3 154690-69-4 154690-70-7
154690-71-8 154690-72-9
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; homol. of human interleukin-1.beta.-convertase with Caenorhabditis elegans ced-3 and mouse NEDD-2 and inhibition of cell death)

L79 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:264626 HCAPLUS
DN **120:264626**
TI Inhibitors of ced-3 and related proteins
IN Horvitz, H. Robert; Yuan, Junying; Shaham, Shai
PA Massachusetts Institute of Technology, USA
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-57
ICS C12N009-64; C12N015-39; A61K031-70; A61K037-02; C12Q001-68; G01N033-577; G01N033-68
CC 7-3 (Enzymes)
Section cross-reference(s): 1, 15
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9325694	A1	19931223	WO 1993-US5705	19930614
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 672151	A1	19950920	EP 1993-915351	19930614
	R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08500482	T2	19960123	JP 1993-501786	19930614
PRAI	US 1992-897788		19920612		
	US 1992-984182		19921120		
	WO 1993-US5705		19930614		

AB Human interleukin-1.beta. convertase (ICE) is structurally similar to the protein encoded by the C. elegans cell death gene, ced-3. Comparative and mutational analyses of the two proteins, together with previous observations, suggest that the Ced-3 protein may be a cysteine protease like ICE and that ICE may be a human equiv. of the nematode cell death gene. Another mammalian protein, the murine NEDD-2 protein, was also found to be similar to Ced-3. The NEDD-2 gene is implicated in the development of the murine central nervous system. On the basis of these findings, novel drugs for enhancing or inhibiting the activity of ICE, ced-3, or related genes are provided. Such drugs may be useful for treating inflammatory diseases and/or diseases characterized by cell deaths, as well as cancers, autoimmune disorders, infections, and **hair growth** and **hair loss**.
Furthermore, such drugs may be useful for controlling pests, parasites and genetically engineered organisms. Furthermore, novel inhibitors of the activity of ced-3, ICe and related genes are described which comprise portions of the genes or their encoded products.

ST ced3 interleukin converting enzyme similarity inhibitor; nedd2 ced3 gene enzyme similarity; cysteine proteinase inhibitor CED3 ICE NEDD2; cell death control ced3 protein analog

IT Gene, animal
RL: BIOL (Biological study)
(NEDD-2, of mouse, similarity to ced-3 gene of Caenorhabditis of, in design of inhibitors of programmed cell death)

IT **Alopecia**
Hypoxia
Infection

(cell death in, prevention of, cell death-inhibiting derivs. of ced-3 and related proteins for)
IT Neoplasm inhibitors
Parasiticides
(cell proliferation-inhibiting derivs. of ced-3 and related proteins as)
IT Proteins, specific or class
RL: BIOL (Biological study)
(gene crmA, of cowpox virus, as inhibitor of ced-3 and related proteins, for prevention of cell death)
IT Inflammation inhibitors
(inhibitors of ced-3 and related proteins as, prevention of cell death in relation to)
IT Cell proliferation
(inhibitors of, ced-3 and related proteins as, stimulation of cell death in relation to)
IT Genetic element
RL: BIOL (Biological study)
(Tc1 element, RFLP assocd. with, near ced-3 gene of Caenorhabditis elegans)
IT Antibodies
RL: BIOL (Biological study)
(auto-, cells producing, inhibition of proliferation of, cell proliferation-inhibiting derivs. of ced-3 and related proteins as)
IT Gene, animal
RL: BIOL (Biological study)
(ced-3, cloning of, similarity of gene product to interleukin 1.beta. convertase, inhibitors of ced-3 protein and convertase activity in relation to)
IT Death
(cell, inhibitors of, peptides from ced-3 protein and interleukin 1.beta. converting enzyme as, gene fragments in relation to)
IT Gene
RL: PREP (Preparation)
(chimeric, of ced-3 of Caenorhabditis elegans and lacZ of Escherichia coli, in prepn. inhibitors of ced-3 function)
IT Virus, animal
(cowpox, crmA protein of, as inhibitor of ced-3 and related proteins, for prevention of cell death)
IT Disease
(degenerative, cell death in, prevention of, cell death-inhibiting derivs. of ced-3 and related proteins for)
IT **Hair**
(**follicle**, proliferation of, inhibition of, cell proliferation-inhibiting derivs. of ced-3 and related proteins as)
IT Heart, disease
(infarction, cell death in, prevention of, cell death-inhibiting derivs. of ced-3 and related proteins for)
IT Brain, disease
(injury, cell death in, prevention of, cell death-inhibiting derivs. of ced-3 and related proteins for)
IT **Aldehydes**, biological studies
RL: BIOL (Biological study)
(**peptide**, as inhibitors of ced-3 and related proteins, for prevention of cell death)
IT Genetic polymorphism
(restriction fragment length, assocd. with ced-3 gene of Caenorhabditis elegans)
IT Brain, disease
(stroke, cell death in, prevention of, cell death-inhibiting derivs. of ced-3 and related proteins for)
IT 37353-41-6, Cysteine proteinase
RL: BIOL (Biological study)
(Ced-3 protein and interleukin-1.beta.-converting enzyme and NEDD-2 protein as, stimulation and inhibition of cell death in relation to)
IT 154250-82-5 154250-83-6 154250-84-7 154690-73-0 154690-74-1

154690-75-2 154690-76-3 154690-77-4 154690-78-5 154690-79-6
RL: PRP (Properties); BIOL (Biological study)
(amino acid sequence of)
IT 154690-61-6, Protein NEDD 2 (mouse reduced) 154690-61-6D, Protein NEDD 2 (mouse reduced), amino acid-substituted analogs
RL: PRP (Properties); BIOL (Biological study)
(amino acid sequence of, as modulator of cell death)
IT 138862-09-6
RL: PRP (Properties); BIOL (Biological study)
(amino acid sequence of, similarity to ced-3 gene product of)
IT 154690-50-3
RL: PRP (Properties); BIOL (Biological study)
(amino acid sequence of, similarity to interleukin-1.beta. converting enzyme of, design of inhibitors in relation to)
IT 143313-51-3
RL: BIOL (Biological study)
(as inhibitor of ced-3 and related proteins, for prevention of cell death)
IT 154690-51-4 154690-52-5 154690-53-6 154690-54-7
RL: BIOL (Biological study)
(as inhibitor of ced-3 function)
IT 9031-11-2D, .beta.-Galactosidase, fusion products with ced-3 gene products
RL: BIOL (Biological study)
(as inhibitor of ced-3-mediated cell death)
IT 122191-40-6D, Interleukin 1.beta. convertase, amino acid substituted analogs
RL: BIOL (Biological study)
(as modulators of cell death)
IT 154690-55-8 154690-56-9 154690-57-0 154690-58-1 154690-59-2 154690-60-5
RL: BIOL (Biological study)
(as stimulator of cell death)
IT 154690-48-9 154690-49-0
RL: BIOL (Biological study)
(in prepn. inhibitors of ced-3 function)
IT 153517-58-9
RL: PRP (Properties); BIOL (Biological study)
(nucleotide sequence and cloning of)
IT 138861-51-5 154690-62-7 154690-63-8 154690-64-9 154690-65-0 154690-66-1 154690-67-2 154690-68-3 154690-69-4 154690-70-7 154690-71-8 154690-72-9
RL: PRP (Properties); BIOL (Biological study)
(nucleotide sequence of)
IT 153604-27-4 153604-28-5 153604-29-6 153604-30-9 153604-31-0 153604-32-1 153604-33-2
RL: BIOL (Biological study)
(**peptide aldehydes** contg., as inhibitors of ced-3 and related proteins, for prevention of cell death)
IT 122191-40-6, Interleukin 1.beta. convertase
RL: BIOL (Biological study)
(similarity to Ced-3 gene product of Caenorhabditis elegans of, control of cell death in relation to)

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MOST RECENT DERWENT UPDATE 200223 <200223/DW>
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L125 ANSWER 1 OF 2 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2000-686989 [67] WPIX
DNC C2000-208928
TI Identifying a compound effective in treating multiple myeloma and myeloma bone disease, involves subjecting the compound to an assay determining its ability to inhibit NF-kB or **proteasomal** activity.
DC B04
IN **MUNDY, G R**
PA (OSTE-N) **OSTEOSCREEN INC**
CYC 22
PI WO 2000061167 A2 20001019 (200067)* EN 22p A61K038-04
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP
AU 2000042040 A 20001114 (200108) A61K038-04
EP 1169049 A2 20020109 (200205) EN A61K038-04
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 2000061167 A2 WO 2000-US9121 20000407; AU 2000042040 A AU 2000-42040 20000407; EP 1169049 A2 EP 2000-921764 20000407, WO 2000-US9121 20000407
FDT AU 2000042040 A Based on WO 200061167; EP 1169049 A2 Based on WO 200061167
PRAI US 1999-289229 19990409
IC ICM A61K038-04
ICS A61K031-166; A61K031-40; A61P019-08
AB WO 200061167 A UPAB: 20001223
NOVELTY - Identifying a compound (I) effective in treating myeloma bone disease involves subjecting the compound to an assay to determine its ability to inhibit transcription factor NF-kB activity or production, or to an assay to determine its ability to inhibit **proteasomal** enzyme activity or production.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) a pharmaceutical composition for treating myeloma bone disease comprising (I); and
(2) a method of treating myeloma bone disease by the administration of (I).
ACTIVITY - Osteopathic; cytostatic.
Nine C57BL/KaLwRij mice were inoculated with 0.5 asterisk 106 5TGM-1 cultured myeloma cells and tumor volume was assessed by the formula Tumor volume (cm3) = 4/3((length + width)-1)/2. The mice with tumors were randomized into two groups and treatment was commenced on day 35. One group has PSI injected directly into the tumors and the other group has only vehicle injected into the tumors. The tumors in the latter group (untreated mice) continued to grow, resulting in the mice dying between 42 and 55 days after myeloma cell inoculation. The size of the tumors in the treated mice decreased markedly and the mice remained healthy up to 3 months after tumor inoculation, even though treatment was discontinued. The result showed that the treated mice were alive and well with no signs of tumor 4 months after treatment.
MECHANISM OF ACTION - Inhibitor of NF-kB activity; inhibitor of **proteasomal** activity.
(I) reduces myeloma tumor volume, delays onset of limb paralysis, decreases the viability of myeloma cells and reduces the volume of tumor marker, IbG2b. (claimed).
USE - (I) is useful for treating multiple myeloma such as osteopenia, osteolytic lesions, osteopetrosis, bone fracture and osteolytic bone

disease, and myeloma bone disease (claimed).
Dwg.0/6
FS CPI
FA AB; DCN
MC CPI: B04-C01A; B10-A06; B10-A12A; B14-H01; B14-H01A; B14-L06

L125 ANSWER 2 OF 2 WPIX COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2000-171065 [15] WPIX
DNC C2000-053186
TI Compound that inhibits the activity of NF-kappa B useful for enhancing bone formation.
DC B04 B05
IN **GARRETT, I R; MUNDY, G R; ROSSINI, G**
PA (OSTE-N) **OSTEOSCREEN**; (OSTE-N) **OSTEOSCREEN INC**
CYC 73
PI WO 2000002548 A2 20000120 (200015)* EN 37p A61K031-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AL AM AU BA BB BG BR CA CN CU CZ EE GE HU IL IN IS JP KP KR LC LK LR LT LV MD MG MK MN MX NO NZ PL RO SD SG SI SK TR TT US UZ VN
AU 9963109 A 20000201 (200028) A61K031-00
EP 1096924 A1 20010509 (200128) EN A61K031-00
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 2000002548 A2 WO 1999-US15533 19990709; AU 9963109 A AU 1999-63109 19990709; EP 1096924 A1 EP 1999-933827 19990709, WO 1999-US15533 19990709
FDT AU 9963109 A Based on WO 200002548; EP 1096924 A1 Based on WO 200002548
PRAI US 1998-113947 19980710
IC ICM A61K031-00
AB WO 200002548 A UPAB: 20000323
NOVELTY - Enhancing bone formation, treating pathological dental conditions, treating degenerative joint conditions by administration of NF-kappa B inhibitor.

DETAILED DESCRIPTION - Enhancing bone formation or treating pathological dental conditions or treating degenerative joint conditions in a vertebrate animal comprises administration of a compound that inhibits the activity of NF-kB or that inhibits **proteasomal** activity or that inhibits production of **proteasome** proteins.

INDEPENDENT CLAIMS are included for the following:

(1) treatment of a condition benefited by stimulating **hair** growth comprising administration of a compound that inhibits the activity of NF-kB or that inhibits **proteasomal** activity or that inhibits production of these proteins, and

(2) identifying a compound which enhances bone growth or stimulates **hair** growth comprising subjecting a candidate compound to an assay to assess its ability to inhibit:

(a) NF-kB activity, or

(b) the production of NF-kB, or

(c) **proteasomal** activity, or

(d) the production of enzymes with **proteasomal** activity,

where for all the inhibitory compound is identified as a compound that enhances bone growth.

ACTIVITY - Osteopathic; Endocrine-Gen.; Screening; Vulnerary. PSI (N-carbobenzoyl-Ile-Glu-(OtBu)-Ala-Leu-CHO) was assayed in vitro for calvarial bone growth. Administered at 0.1, 1 and 5 mg/kg/day, the % increase in bone area compared to control was 21.7, 35.4 and 32.1%, respectively. The 1 and 5 mg/kg/day doses produced an increase in new bone width of 19.9%.

MECHANISM OF ACTION - Antimetastatic; Nuclear-Factor-Inhibitor-Kappa-B.

USE - The method can be used for enhancing bone formation, treating pathological dental conditions, degenerative bone conditions, osteoporosis, bone fracture or deficiency, primary or secondary hyperparathyroidism, periodontal disease or defect, metastatic bone disease, osteolytic bone disease, post-plastic surgery, post-prosthetic joint surgery, and post-dental implantation, and for stimulating **hair** growth (claimed). The compounds may also be useful in wound

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     healing or tissue repair.
          ADVANTAGE - None given.
     Dwg.0/1
FS   CPI
FA   AB; DCN
MC   CPI: B04-C01; B06-D13; B06-F05; B07-A02B; B07-D03; B10-A06; B10-A10;
          B10-D02; B11-C08; B12-K04A; B14-D03; B14-N01; B14-N06; B14-N11;
          B14-N17B; B14-R02
TECH                UPTX: 20000323
     TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The compound does
     not inhibit the isoprenoid pathway. The compound is lactacystin, a
     peptidyl aldehyde or PTX. The method further comprises
     administration of one or more agents that promote bone growth or that
     inhibit bone resorption such as bone morphogenetic factors,
     anti-resorptive agents, osteogenic factors, cartilage-derived
     morphogenetic proteins, growth hormones, estrogens, bis phosphonates,
     statins or differentiating factors.


=> d his

     (FILE 'HOME' ENTERED AT 13:27:40 ON 16 APR 2002)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 13:27:51 ON 16 APR 2002
               E MG 132/CN
L1           1 S E3
               E MG 115/CN
L2           1 S E3
               E MG 101/CN
L3           1 S E3
               E C26H41N3O5/MF
L4          30 S E3 AND 46.150.18/RID AND 1/NR
L5          11 S L4 AND FORMYL
L6           8 S L5 AND LEUCYL
L7           6 S L6 NOT ISOLEUCINAMIDE
L8           5 S L7 AND PHENYLMETHOXY
               E C25H39N3O5/MF
L9           2 S E3 AND 46.150.18/RID AND 1/NR AND LEUCINAMIDE AND PHENYLMETHO
               E C20H37N3O4/MF
L10         11 S E3 AND LEUCINAMIDE AND LEUCYL
L11          5 S L10 AND FORMYL
L12          9 S L8,L9,L11 NOT L1-L3
L13          1 S 140879-24-9
L14          3 S L1-L3
               SEL RN
L15          0 S E1-E3/CRN

     FILE 'HCAPLUS' ENTERED AT 13:33:36 ON 16 APR 2002
L16        241 S L14
L17        431 S MG()(132 OR 115 OR 101) OR MG132 OR MG115 OR MG101
L18        157 S CALPAIN INHIBITOR()(1 OR I)
L19        687 S L16-L18
L20         25 S L12
L21       1475 S (PEPTIDE OR PEPTIDYL)(L)(ALDEHYDE OR ALDEHYDIC)
L22          7 S (PEPTIDE OR PEPTIDYL)(L)EPOXY(L)KETONE
L23       3055 S L13
L24       4717 S PROTEASOM?
L25        304 S (26S OR 26 S)(L)(PROTEASE OR PROTEINASE)
L26        774 S MULTICATALYTIC(L)(PROTEASE OR PROTEINASE)
L27         21 S TRICORN(L)(PROTEASE OR PROTEINASE)
L28         49 S IMMUNOPROTEASOM?
L29          9 S IMMUNO PROTEASOM?
L30        105 S PROSOME
L31          2 S IMMUNOPROTEOSOM?
L32          2 S IMMUNO PROTEOSOM?
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L33        5020 S L23-L32
L34        1481 S L21,L22
L35         694 S L19,L20
L36        4396 S ALOPEC? OR BALD OR BALDING OR BALDNESS
L37        3041 S SCALP?
L38        5442 S HAIR(L)(LOSS OR LOSE OR LOSING OR LOST OR GROW? OF THIN? OR S
                E HAIR/CT
                E E31+ALL
L39        1419 S E1,E2
                E HAIR/CT
L40        1409 S E6,E8,E9,E13,E15,E16
                E E37+ALL
L41        1329 S E1,E2
                E HAIR GROWTH/CT
                E E7+ALL
                E E1
                E E10+ALL
L42       15395 S E2+NT
                E E9+ALL
L43       18926 S E6,E5+NT
L44         824 S E20+NT
                E HAIR/CT
L45         603 S E24
L46          40 S E26
L47          73 S E32
L48          42 S E39
L49          56 S E42
                E E26+ALL
L50         289 S E2
                E HAIR PREPARATION/CT
L51        4002 S E7,E8,E9,E10,E13,E15-E23
L52        8270 S SHAMPOO?
                E KERATIN/CT
                E E18+ALL
                E E1
                E E17+ALL
L53           3 S L35 AND L36-L52
L54           2 S L53 NOT HYPOXIA
L55           7 S L33 AND L36-L52
L56           6 S L34 AND L36-L52
L57          12 S L54-L56
L58         819 S (26S OR 26 S)(L)(PROTEASOM? OR PROTEOSOM?)
L59           4 S L58 AND L36-L52
L60          12 S L57,L59
                SEL DN 1 4 5 9 10 11 L60
L61           6 S L60 AND E1-E6
                E MUNDY G/AU
L62         259 S E3,E6-E10
                E GARRETT I/AU
L63          53 S E3-E7
L64          55 S E239
L65           7 S E309,E310
                E GOSSINI G/AU
                E ROSSINI G/AU
L66          80 S E3-E16
L67           2 S L35 AND L62-L66
L68           1 S L34 AND L62-L66
L69           4 S L33 AND L62-L66
L70           8 S L61,L67-L69
                E OSTEOSCREEN/PA,CS
L71          13 S E3-E12
L72           3 S L71 AND L33-L35
L73           8 S L70,L72
L74           7 S L73 AND (HAIR OR BALD? OR ALOPEC? OR SHAMPOO OR FOLLIC? OR SH
L75           8 S L73,L74
L76           2 S L75 AND (GROWTH FACTOR)(L)(EPIDERM? OR FIBROBLAST? OR PLATELE
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L77           0 S L75 AND (PARATHYROID OR LEUKEM?)
L78           3 S L75 AND GROWTH? FACTOR?
L79           8 S L75,L76,L78
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 14:06:56 ON 16 APR 2002
L80           4 S E1-E4

     FILE 'REGISTRY' ENTERED AT 14:07:17 ON 16 APR 2002

     FILE 'HCAPLUS' ENTERED AT 14:07:28 ON 16 APR 2002

     FILE 'USPATFULL, USPAT2' ENTERED AT 14:07:55 ON 16 APR 2002
L81         284 S L19
L82           1 S L81 AND HAIR?/CT
L83           0 S L81 AND ALOPEC?/CT
L84          30 S L81 AND (HAIR OR ALOPEC? OR BALD OR BALDING OR BALDNESS OR SC
                E A61K007-16/IC,ICM,ICS
                E A61K007-06/IC,ICM,ICS
L85        3230 S E3-E55
L86           1 S L81 AND L85
L87           1 S L82,L86
L88           1 S L84 AND L87
L89          29 S L84 NOT L88

     FILE 'BIOSIS' ENTERED AT 14:13:40 ON 16 APR 2002
L90         591 S L19
L91           1 S L90 AND (HAIR OR ALOPEC? OR BALD OR BALDING OR BALDNESS OR S
L92           6 S L90 AND 185?/CC
L93           0 S L90 AND 22020/CC

     FILE 'MEDLINE' ENTERED AT 14:15:58 ON 16 APR 2002
L94         719 S L19
L95           0 S L20
L96        4151 S L33
L97         640 S L34
                E HAIR/CT
                E E3_ALL
                E HAIR/CT
                E E3+ALL
L98       14575 S E4+NT
                E HAIR/CT
                E E110+ALL
L99       11743 S E4+NT
                E SCALP/CT
                E E3+ALL
L100       5940 S E4+NT
                E SCALP/CT
                E E4+ALL
L101       2273 S E4+NT
L102          0 S L94-L97 AND L98-L101

     FILE 'WPIX' ENTERED AT 14:18:40 ON 16 APR 2002
L103         15 S L17 OR L18
L104        354 S L21,L22
L105        115 S L24-L32,L58
L106      11977 S (P930 OR Q252)/M0,M1,M2,M3,M4,M5,M6
                E A61K007-06/IC,ICM,ICS
L107      16230 S E3-E53
                E A61K007-06/ICA,ICI
L108        489 S E3-E13
                E A61K007:06/ICI
L109          2 S E3,E4
L110      32063 S (D08-B OR D08-B03 OR D08-B04 OR D08-B05 OR D08-B06 OR D08-B07
L111          0 S L106-L110 AND L103
L112         10 S L106-L110 AND L104
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L113          2 S L106-L110 AND L105
L114         11 S L112,L113
                E MUNDY G/AU
L115         21 S E3,E5
                E GARRETT I/AU
L116          6 S E3,E5
L117          9 S E61
                E ROSSINI G/AU
L118          7 S E3-E5
                E OSTEOSCREEN/PA
L119         10 S E3,E4
L120          2 S L103-L105 AND L115-L119
L121          1 S L114 AND L120
L122          2 S L120,L121
L123          7 S L114 AND (HAIR OR ALOPEC? OR BALD?)
L124          1 S L122 AND L123
L125          2 S L122,L124

     FILE 'WPIX' ENTERED AT 14:29:56 ON 16 APR 2002
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